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Effects of Prenatal Combined Stress on Passive Avoidance Learning and Memory in Rats

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The effects of combined prenatal stress (including the action of electromagnetic fields, zoo social stress, and immobility on pregnant females) on the learning and memory of offsprings of rats were investigated. Two groups of male and female rats ($n = 16$ in each) were studied. The animals received prenatally (from 8 to 18 days of gestation) three different stresses as follows: immobilization of pregnant mothers (0.5 h, twice a day by placing in a restrainer), social stress (6 rats kept in a small cage), and exposure to electromagnetic waves (4 h, 0.5 MT, 50 Hz). The learning and memory of rats were assessed two months after birth (2, 6, 24, 48 h and 1- and 2-week-long intervals after training) by using a conditioning avoidance method. Also, expression of the *APP* gene was investigated in rats using RT-PCR. The prenatal stress suppressed visits of male offsprings to the dark compartment in comparison with the control group, and the difference was significant 2 h after the shock ($P < 0.05$). These parameters were also reduced in female offsprings of the stressed group, but this difference was insignificant ($P > 0.05$).The relative expression of the *APP* gene was also higher in both male and female offsprings ($P < 0.05$ and 0.01, respectively). Thus, the implemented combined prenatal stress impaired the acquisition process and long-term memory in male offsprings and long-term memory in female offsprings. Also, it may promote deposition of β-amyloid plaques.

Keywords: memory, learning, prenatal combined stress, Alzheimer's disease, *APP*.

INTRODUCTION

There is evidence pointing to the importance of *in-utero* and early-life periods in mammals on the quality of later life. Good physical and mental conditions during pregnancy are important for the normal development of the baby. Stress is a factor that has always disturbed the person's physical and mental balance and induces psychosomatic and mental problems in different aspects of life. This influence reduces the individual's performance. Prenatal stress can be rather dangerous and is a potential factor involved in the development of some neurological diseases [1, 2]. In this regard, it has been reported that prenatal stress may interfere with brain development, leading to the arrival of abnormal neuronal connections and subsequent brain structural and functional abnormalities. Evidently, children subjected to prenatal stress have a lower birth body mass and smaller head circumferences, which may be a sign of defective brain evolution [3, 4].

The hippocampus occupies an important position in learning mechanisms; there is evidence that *in-utero* stress can have a decisive effect on the development and activity of this brain structure. Chronic stress reduces the number of hippocampal neurons, and one of the mechanisms involved in this event is an increase of neurosteroids in the blood and brain of the fetus [5]. In this context, it has been shown that immobilization stress of the mother's organism causes dysfunction of the hippocampus and disrupts spatial memory formation in borned rats [6, 7]. Some researches showed that the effects

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